Interactions of antibodies with selected antigens – computational modeling

Anna Gogolinska[1,2], Wieslaw Nowak[1]

1) Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University, Toruń, Poland

2) Faculty of Mathematics and Computer Science, Nicolaus Copernicus University, Toruń, Poland

The immune (IS) system is a part of defense against bacteria, viruses and other pathogens. Millions of cells are involved in that activity. Important part of the immune response is the humoral response. Basic elements of that response to antigens invading an organism are antibodies (immunoglobulins, Ig). Igs are Y-shaped proteins and have a common structure, they differ only in an antigen-binding site. The antibodies are extremely specific and interact very strongly with appropriate antigens. In our work we used computer modeling tools to study two antigens: a major grass pollen allergen Phl p 2 and a chemokine MCP-1, both in complexes with their specific human antibodies.

The Phl p 2 and the specific human immunoglobulin E (IgE) had been isolated from a pollen allergic patient [1]. Interactions of that antigen and the antibody induce the IS response and allergic symptoms. Studies of the complex of Phl p 2 and IgE may help in better understanding the allergy. MCP-1 belongs to chemokines - a family of cytokines, that are produced by immune cells. Their main function is chemoattraction. Chemokines recruit immune cells to the place of infection and cause the IS response in that region. MCP-1 is present in central nervous system and its elevated level can be related with autism (ref). Thus our studies of the complex of MCP-1 and antibody could help in diagnosis of autism.

In order to understand molecular recognition processes in atomic detail we performed classical MD [2] simulations of both complexes and then more than 20 of 2 ns SMD simulations [3] of enforced dissociations of the complexes. Different directions rupture forces were tested. We divided their directions into two groups: “vertical” (parallel to the main axis of the antibody) and “lateral”. Our results show that in both complexes the separation the antigen from the antibody in the “vertical” direction requires about 30 % higher values of the force than in the “lateral” direction . We have identified amino acids crucial for interactions between the antigens and the antibodies. Appropriate hydrogen bonds and salt bridges, contribute to the strong specific interactions. The methodology established in this study may help to understand better Lateral Atomic Force experiments, especially related to complexes of fibronectin and its antibody [M. Lekka, A. Kulik, W. Nowak – unpublished results].

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